CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

022370Orig1s000

Trade Name: Tramadol hydrochloride extended-release capsules

Generic Name: Tramadol hydrochloride extended-release capsules

Sponsor: Cipher Pharmaceuticals, Inc.
(c/o) Wilcox and Savage, P.C.
One Commercial Place, Suite 1800
Norfolk, VA 23510

Approval Date: May 7, 2010

Indications: Tramadol hydrochloride extended-release capsules is an opioid agonist indicated for the management of moderate to moderately severe chronic pain in adults who require around-the-clock treatment of their pain for an extended period of time

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APPLICATION NUMBER:

022370Orig1s000

APPROVAL LETTER

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022370 **NDA APPROVAL**

Cipher Pharmaceuticals, Inc.
(c/o) Wilcox and Savage, P.C.
One Commercial Place, Suite 1800
Norfolk, VA 23510

Attention: Conrad M. Shumadine, Esq.
Wilcox and Savage P.C.
U.S. Agent

Dear Mr. Shumadine:

Please refer to your new drug application (NDA) dated April 14, 2008, received April 15, 2008, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for tramadol hydrochloride extended-release capsules 100 mg, 200 mg, and 300 mg.

We acknowledge receipt of your submissions dated May 22, June 27, September 8, October 20, and November 14 and 17, 2008, January 6, February 10, September 16, and December 15, 2009, and January 14, March 5, April 30 and May 4 and 6, 2010.

The March 5, 2010, submission constituted a complete response to our February 13, 2009, action letter.

This new drug application provides for the use of tramadol hydrochloride extended-release capsules for the management of moderate to moderately severe chronic pain in adults who require around-the-clock treatment of their pain for an extended period of time.

We have completed our review of this application, as amended, and it is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text.

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of prescribing information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit, via the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical to the enclosed labeling text for the package insert. Information on submitting SPL

files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

CARTON AND IMMEDIATE CONTAINER LABELS

We acknowledge your May 6, 2010, submission containing final printed carton and container labels. We remind you of your agreement to remove the following statement at the next printing:

Warning: cannot be interchanged with other tramadol extended-release products

PROPRIETARY NAME

If you choose to use a proprietary name for this product, the name and its use in the labels must conform to the specifications under 21 CFR 201.10 and 201.15. We recommend that you submit any proprietary name to the Agency for our review prior to its implementation.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for ages 0 to < 2 years because necessary studies are impossible or highly impracticable. This is because there are too few patients in this age range who require treatment for chronic pain using an oral modified-release analgesic to be able to conduct clinical trials.

We are deferring submission of your pediatric study for ages ≥ 2 to 17 years for this application because this product is ready for approval for use in adults and the pediatric study has not been completed.

Your deferred pediatric study required by section 505B(a) of the Federal Food, Drug, and Cosmetic Act is a required postmarketing study. The status of this postmarketing study must be reported annually according to 21 CFR 314.81 and section 505B(a)(3)(B) of the Federal Food, Drug, and Cosmetic Act. This required study is listed below.

653.1 To study the pharmacokinetics, efficacy and safety of tramadol hydrochloride extended-release capsules for the management of moderate to moderately severe chronic pain in pediatric patients ages ≥ 2 to 17 years.

Final Protocol Submission:	December 2013
Study Start Date:	December 2014
Final Report Submission:	December 2016

Submit final study reports to this NDA. For administrative purposes, all submissions related to this required pediatric postmarketing study must be clearly designated "**Required Pediatric Assessment.**"

EXPIRATION DATING PERIOD

An expiration dating period of 36 months is granted to the 100, 200, and 300 mg tramadol hydrochloride extended-release capsules, stored at 25°C (77°F); excursions permitted between 15°-30°C (59°-86°F).

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

LETTERS TO HEALTH CARE PROFESSIONALS

If you decide to issue a letter communicating important safety-related information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit, at least 24 hours prior to issuing the letter, an electronic copy of the letter to this NDA, to CDERMedWatchSafetyAlerts@fda.hhs.gov, and to the following address:

MedWatch
Food and Drug Administration
Suite 12B-05
5600 Fishers Lane
Rockville, MD 20857

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Kathleen Davies, Senior Regulatory Project Manager, at (301) 796-2205.

Sincerely,

{See appended electronic signature page}

Sharon Hertz, M.D.
Deputy Division Director
Division of Anesthesia and Analgesia Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

ENCLOSURES (2):
Content of Labeling
Carton and Container Labeling

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22370	ORIG-1	CIPHER PHARMACEUTICALS LTD	TRAMADOL HYDROCHLORIDE

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

SHARON H HERTZ
05/07/2010